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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

WALLENHORST, MAUREEN

ART UNIT	PAPER NUMBER
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1743

DATE MAILED: 09/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/853,867

Applicant(s)

KLEE, GEORGE G.

Examiner

Maureen M. Wallenhorst

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-28 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: The citizenship of inventor George Klee is missing.

2. Claims 1-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

On line 4 of claim 1, the phrase "test values from patient specimens" is indefinite since it is not clear whether these test values correspond to values of the same target analyte that was measured in the control pool. See this same problem on line 5 of claim 8, on line 6 of claim 17, on line 7 of claim 26, and on line 8 of claim 27. On lines 2-3 of claim 1, the phrase "wherein the control pools have" should be changed to "wherein the control pool has"—since only one commutable control pool was previously recited. This same change should also be made on lines 3-4 of claim 8, on lines 4-5 of claim 17, on lines 5-6 of claim 26, on lines 6-7 of claim 27, and on lines 2-3 of claim 28.

In claims 3-4, the phrase "the normalized distribution of the patient specimen data" lacks antecedent basis since claim 1 does not recite that the distribution of patient specimen data is normalized. See this same problem in claims 10-11 and 19-20.

On line 8 of claim 7, the "patient test values" are indefinite since it is not clear whether these values are for the same target analyte that was measured in the control pool. In part e) of claim 7, the phrase "the analytical instrument" should be changed to "the clinical laboratory instrument"—so as to be consistent with the preamble of the claim.

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On the last line of claim 8, the phrase "the instrument" lacks antecedent basis. See this same problem on the last line of claim 17.

In the preamble of claims 9-16, the phrase "the program" should be changed to -the computer readable medium—since claim 8, from which claims 9-16 ultimately depend, recites a computer readable medium.

Claim 11 is indefinite since it depends from claim 10 and recites the same limitation as claim 10. Therefore, claim 11 fails to further limit claim 10.

In claim 14, the phrase "the calibration control signal" lacks antecedent basis since claim 14 depends from claim 8. See this same problem in claim 23.

On line 2 of claim 16, it is unclear what "residual RMS error" refers to. See this same problem in claim 25.

Claim 19 is indefinite since it depends from itself.

Claim 20 is indefinite since it depends from claim 19 and recites the same limitation as claim 19. Therefore, claim 20 fails to further limit claim 19.

On the last line of claim 26, the phrase "the instrument" should be changed to -the instrumentation system—so as to be consistent with the language used in the preamble of the claim.

On line 4 of claim 28, the "patient distribution index" is indefinite since it is not clear whether this index contains values for the same target analytes that were measured in the control pool.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35

U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klee (from Clinica Chimica Acta, submitted in the Information Disclosure Statement filed on September 4, 2001) in view of Smith et al (from Clinical Chemistry, also submitted in the Information Disclosure Statement filed on September 4, 2001).

Klee teaches of a method for establishing tolerance limits for analytic bias and imprecision based on variations in population test distributions. The aim of the method taught by Klee is to assure that the analytic shifts of laboratory measurements are smaller than the population shifts caused by other factors in the system such as differences between patients and biologic changes within patients. The steps of the method for determining tolerance limits for analytic bias include establishing a normalized (Gaussian) distribution of patient specimen data (see step 1 on page 181 of Klee), forming control pool data with controls having known values for target analytes (i.e prostate-specific antigen, PSA, see abstract and step 2 on page 181 of Klee), and determining tolerance limits from the control pool data and the patient distributions (see steps 3-8 on pages 181-182 of Klee). Klee teaches that it is important to form tolerance

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limits for the measurements of target analytes in both patient and control pools, and to detect shifts or analytic bias with respect to these tolerance limits since these shifts or bias can substantially alter medical practice parameters, especially by increases in false positives which subject many patients to further investigations. Klee fails to teach of adjusting the calibration of the measurement instrument used to measure the target analytes (i.e. PSA) in the patient specimens and the control pool with respect to the tolerance limits to compensate for any analytic bias from the tolerance limits.

Smith et al also teach of a method for detecting analytic bias from an established reference range of values (i.e. tolerance limits) for target analytes using patient samples. Smith et al teach that analytic systems can be monitored for quality control by the continuous comparison of a distribution of patient data to a distribution of control data. Smith et al teach that previously, automated laboratory instruments were recalibrated based upon an error signal from a known-value control. See the last paragraph on page 263 of Smith et al. However, Smith et al suggests that in the continuous comparison method of quality control between patient data distributions and control data distributions, that analytic bias (i.e. the values or tolerance limits outside of an established range) can be used as an error signal in place of the previously-used erroneous known-value control signals to adjust the calibration of the automated laboratory instrument used to measure both the patient and control samples. Smith et al also teach of a computer-readable medium/program for running a quality control procedure in an analyzer by analyzing both pools of control and patient samples and forming distributions of the resulting data. See the second column on page 258 of Smith et al.

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Based upon a combination of Klee and Smith et al, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to use the analytic bias outside of the tolerance limits taught by Klee as a basis for adjusting the calibration of the instrument or analyzer used to calculate target analyte values for both patient and control samples since Smith et al suggests that analytic bias (i.e. values or tolerance limits outside an established range) can be used as an error signal to adjust the calibration of analytical instruments that measure target analytes in patient and control samples. It also would have been obvious to one of ordinary skill in the art to incorporate the steps taught by Klee for determining appropriate tolerance limits for analytic bias into a computer program since Smith et al teach that a calibration or quality control procedure based upon the analytic bias of patient and control values from an established reference range can be programmed into a computer readable medium/program and run in a computer connected to an analyzer performing measurements on patient and control samples.

6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Please make note of: Salpeter who teaches of a method for calibrating an automatic chemical analyzer, wherein the calibration is adjusted based upon measured changes in the system.

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7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maureen M. Wallenhorst whose telephone number is 703-308-3912. The examiner can normally be reached on Monday-Wednesday from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden, can be reached on (703) 308-4037. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0661.

Maureen M. Wallenhorst
Primary Examiner
Art Unit 1743

mmw

September 2, 2003

Maureen M. Wallenhorst
MAUREEN M. WALLENHORST
PRIMARY EXAMINER
GROUP 1700